Paroxysmal epileptic laryngospasms

Frequent nightly awakenings

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A 19-year-old right-handed man presented with a 3-year history of nocturnal throat constriction with drooling and discomfort. Initially, episodes were exclusively during sleep, 6–7 times per night, but evolved to include infrequent episodes while awake. He was evaluated on several occasions by gastroenterology, and esophageal manometry, nocturnal pH-metry, and esophagogastroduodenoscopy were performed. All tests were unrevealing, except for an esophagogastric junction outflow obstruction. He was prescribed omeprazole, but had no improvement in symptoms. Overnight polysomnography was performed and showed that his events arose out of stage II sleep and resulted in obstructive apnea. Over the ensuing years, he was evaluated by multiple otolaryngologists and allergists with multiple tests including video fiber optic laryngoscopy, all of which were unrevealing. Relaxation and breathing techniques were recommended for episodic laryngospasm by otolaryngologists, but failed to improve symptoms.

Eventually, the patient had one of his typical events accompanied by jerking movements of his upper torso without loss of consciousness, leading to his referral to the neurology clinic. At presentation, his neurologic examination, 3T brain MRI, and brain FDG-PET were normal. He was admitted to the epilepsy monitoring unit (EMU). In the EMU, he had innumerable habitual clinical events characterized by sudden awakening from sleep with feeling of throat constriction, hypermotor behavior, and excessive drooling, all without clear loss of awareness (video 1). Each episode lasted less than 1 minute and a majority (>80%) arose out of stage II sleep. These events were without EEG correlate (figure). The hypermotor semiology, symptoms arising out of sleep, and the stereotyped nature suggested the possibility of epileptic laryngospasms despite the lack of EEG correlate. Therefore, an ictal and interictal ^{99m}Tc -labeled ethyl cysteinate dimer SPECT study was obtained. Ictal–interictal SPECT analyzed by statistical parametric mapping (SPM)¹ revealed ictal hyperperfusion within the left frontoparietal operculum in the region of the ventral sensorimotor cortex, specifically the motor area for nonspeech laryngeal motor function (figure). The patient was diagnosed with apparent epileptic laryngospasm and was discharged home on carbamazepine titration to a target dose of 400 mg twice a day. On follow-up 3 weeks later, the patient reported having uninterrupted sleep for the first time in 3 years. At 6-month follow-up, the patient reported a 90% reduction in events, with milder symptoms during events.

Discussion

Paroxysmal laryngospasm (PL) is uncommon and is defined as an exaggerated response to closure reflex or glottic muscle spasm. The differential diagnosis of paroxysmal laryngospasm is vast (table), and involves many specialties including neurology, otorhinolaryngology, gastroenterology, and psychiatry.

PRACTICAL IMPLICATIONS

Early consideration of seizures arising from the frontal operculum manifesting as nocturnal paroxysmal laryngospasm is critical, since the condition can go undiagnosed, resulting in considerable disruption in restorative sleep and daily function.

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Figure Hyperperfusion in the left fronto-opercular region during an epileptic laryngospasm

Ictal-interictal SPECT analyzed by statistical parametric mapping shows hyperperfusion in the left frontoparietal operculum in the region of the ventral sensorimotor cortex: sagittal (A), coronal (B), and axial (C) view. (D) 3D-rendered SPM data with an approximated position of the split laryngeal sensorimotor organization. Ictal EEG clip in a bipolar montage shows stage II sleep architecture (sleep spindles, V-waves, and K-complex) before the emergence of motion-related muscle artifact during a typical epileptic laryngospasm (E). Of note, 3T seizure protocol MRI was unrevealing (data not shown).

Table Differential diagnosis of paroxysmal laryngospasms

Neurologic disorders ^{2,3}
Epileptic laryngospasms (seizures arising from the frontal operculum)
Multisystem atrophy with nocturnal laryngeal stridor
Sleep disorder ²
Obstructive sleep apnea
Sleep-related choking syndrome
Otolaryngology ³
Laryngeal dystonia
Paradoxical vocal fold motion
Laryngeal paralysis
Gastroesophageal reflux disease ⁷
Globus pharyngeus (functional gastrointestinal disorder) ⁷
Psychogenic laryngospasm ²
Nocturnal panic attacks ²
Others ³
Exercise-induced
Allergic (asthma)
Infectious (whooping cough)

PL as an isolated manifestation of an epileptic disorder is rare.^{2,3} Herein, we present a case of antiepileptic drug (AED)–responsive epileptic laryngospasms with imaging confirmation of ictal hyperperfusion within the left frontoparietal operculum. Seizures arising from the frontal operculum classically include throat constriction, sialorrhea, facial jerking, and dysesthetic burning.³ Although the exact mechanism remains unclear, it is possible that seizures could cause ictal laryngospasms by spreading via autonomic medullary motor regions to the laryngeal branches of the vagus nerve.⁴ The treatment options for epileptic laryngospasm are similar to other focal epilepsies, with previous case reports suggesting a favorable response to carbamazepine.³ Focal resection has been reported for those refractory to AEDs.² The consequences of ictal laryngospasm are typically limited to the discomfort and interruption in sleep and daily function. However, there may be a connection between ictal laryngospasm, obstructive apnea, and the potential for sudden unexplained death in epilepsy.⁴

The ventral sensorimotor cortex (vSMC) has unique neuro-anatomical variances compared with the dorsal sensorimotor cortex (dSMC).⁵ Broadly, the rostral–caudal organization of the vocal tract (from lips, tongue, and larynx) is reflected in the rostral–caudal arrangement of the vSMC; however, some critical distinctions are present.^{5,6} Electrophysiologic studies have shown a split representation of the larynx in humans.⁵ As in nonhuman primates, primary sensorimotor innervation of the larynx has been shown within the ventral-most portion of

the vSMC.^{5,6} However, an additional laryngeal motor representation not present in nonhuman primates has been shown immediately dorsal to lip and tongue motor areas in the dorsal aspect of the vSMC.^{5,6} SPM-SPECT in our case illustrated ictal hyperperfusion localized to the expected region of the more ventral laryngeal sensorimotor region responsible for nonspeech laryngeal motor function, and correlates well with the patient's clinical symptoms.

This case highlights the importance of early consideration of seizures arising from the frontal operculum as a cause of paroxysmal laryngospasm, despite lack of EEG correlate. Lack of EEG correlate should not dissuade the clinician from a diagnosis of epilepsy, as absence of ictal correlate is not uncommon in sleep-related frontal lobe epilepsy. The positive SPECT correlation with the patient's symptoms further illustrates the potential utility of ictal SPECT in diagnosis of this entity. Early diagnosis and treatment minimizes frequent disruption in sleep and impaired daily function that accompanies this uncommon and disabling disease.

Author contributions

R.J. Cannistraro: drafting of the manuscript, acquisition of data, manuscript preparation and literature review. E.H. Middlebrooks: study concept and design, acquisition of data, analysis and interpretation of data, manuscript preparation and literature review, critical revision of the manuscript for important intellectual content. B.H. Brinkmann: acquisition of data, analysis and interpretation of data, critical revision of the manuscript for important intellectual content. A.M. Feyissa: drafting of the manuscript, study concept and design, acquisition of data, analysis and interpretation of data, manuscript preparation and literature review, critical revision of the manuscript for important intellectual content.

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